

REMARKS/ARGUMENTS

With this amendment, claims 1 and 15-26 are pending. New claim 27 is added. Claims 3-9 and 11-13 are withdrawn. Claims 2, 10, and 14 are cancelled without prejudice to subsequent revival. For convenience, the Examiner's rejections are addressed in the order presented in a February 13, 2004 Office Action.

I. Status of the claims

Claim 1 is amended to recite that the beneficial gene is a polymorphism in a CCR5 gene. Support for this amendment is found throughout the application, for example, at page 8, lines 21-27. Claim 1 is also amended to recite that a human is treated for an HIV infection and that cells are obtained from a human donor. Support for this amendment is found throughout the specification, for example, at page 9, lines 16-17. These amendments add no new matter.

Claims 15-17 previously depended from now cancelled claim 14. Claims 15-17 are amended to depend from claim 1. This amendment adds no new matter.

New claim 27 is added and is directed to using umbilical cord blood as a source of stem cells. Support for this amendment is found throughout the application, for example, at page 9, lines 21-22; at Examples 1 and 2, pages 13-14; and at original claim 18. This amendment adds no new matter.

Claims 3-9 and 11-13 are withdrawn. Claims 2, 10, and 14 are cancelled without prejudice to subsequent revival.

II. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1, 2, 10 and 14-26 are rejected under 35 U.S.C. §112, first paragraph because, allegedly, the specification does not enable the full scope of the claims. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

The Examiner appears to have focused improperly on inoperative embodiments, leading to the conclusion that undue experimentation would be required to identify biologically

active enzymes and their encoding nucleic acids of the claimed invention. However, the proper test of enablement is “whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation” (*see, e.g.*, MPEP §2164.01). In the present application, one of skill would know how to avoid inoperative embodiments and to practice the claimed methods, without undue experimentation (*see, In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971)). Moreover, the present application provides guidance in the form of examples for identification of stem cells with beneficial genes and for methods of treatment of HIV using transplanted stem cells.

Claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. As described by the court in *In re Cook and Merigold*, 169 USPQ 302:

Many patented claims read on vast numbers of inoperative embodiments in the trivial sense that they can and do omit ‘factors which must be presumed to be within the level of ordinary skill in the art’ There is nothing wrong with this so long as it would be obvious to one of ordinary skill in the relevant art how to include those factors in such a manner as to make the embodiment operative rather than inoperative.

See, In re Cook and Merigold, 169 USPQ at 302 (quoting in part *In re Skrivan*, 166 USPQ 85, 88 (C.C.P.A. 1970)).

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention (*see, Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)). As described in *Wands*, “a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction

in which the experimentation should proceed” (*see, Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982)).

The claims are amended to recite the use of stem cells comprising a beneficial polymorphism of the CCR5 gene. Methods of detecting such polymorphisms are found throughout the specification, and include hybridization and immunoassays found at page 10, line 20 through page 11, line 10. The hybridization and immunoassays are well known to those of skill.

The Office Action also alleges that there is no guidance for methods of treating patients using stem cells that comprise beneficial genes. Bone marrow transplantation of stem cells comprising beneficial genes for treatment of HIV is no different than bone marrow treatment of other disorders. Bone marrow transplantation is described in the specification at page 12, lines 14-15. Applicants respectfully bring to the Examiner's attention that bone marrow transplantation between allogeneic donor/recipient pairs has been successfully performed since 1968. Bone marrow transplantation between unrelated donor/recipient pairs have been successfully performed since 1977. Chapters of medical textbooks are devoted to the technique. *See, e.g., Smith, B. Stem Cell Transplantation*, in *Cancer: Principles & Practice of Oncology* DeVita *et al.* Eds. (1997). Thus, given the well known nature of bone marrow transplantation in the medical field, the description provided by the specification is more than sufficient.

The Office Action also alleges that working models are necessary to meet the enablement requirement. The specification provides predictive examples of the use of stem cells comprising beneficial genes to treat HIV. *See, e.g., Examples 1 and 2*, pages 13-14. Moreover, proof of the efficacy of stem cells comprising beneficial polymorphisms for treatment of HIV infections is found in the art of record that humans who naturally have such genes have no or delayed onset of AIDS after repeated exposure to the HIV virus. *See, e.g., Carrington et al.* (1999); O'Brien and Dean (1997); and McDermott *et al.* (1998).

The Office Action also alleges that the claims are not enabled because the specification fails to teach ex vivo expansion of stem cells and also alleges that such expansion is required for operation of the claimed methods. Applicants respectfully assert that the claimed methods work using the disclosed methods of stem cell isolation. For example, one unit of

umbilical cord blood will provide sufficient stem cells to transplant most small to average size humans. Large banks of cord blood are currently available for transplantation. If additional cells are need for transplantation, they can be isolated after an appropriate bone marrow donor is identified.

The Office Action alleges that the claimed invention is not enabled for xenogeneic transplantation. In order to expedite prosecution, the claims are now amended to recite treatment of a human using stem cells from a human donor.

In view of the above amendments and remarks, Applicants respectfully request that the rejection for alleged lack of enablement be withdrawn.

III. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 1, 2, 10, and 18-26 are rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. According to the Office Action, the specification lacks description of the claimed invention, such that a skilled artisan would recognize that Applicants had possession of the claimed invention at the time of filing. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

In order to expedite prosecution, claim 1 is amended to recite that the beneficial gene is a polymorphism in the CCR5 gene. In view of this amendment, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

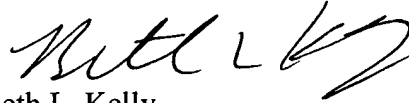
In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

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PATENT

Respectfully submitted,



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